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L55  ANSWER 1 OF 10  WPIX COPYRIGHT 2007       THE THOMSON CORP on STN
AN   2004-375904 [35]   WPIX  Full-text
DNC  C2004-141379 [35]
TI   Preparation of 3-hydroxy-5-beta-H-steroidal sapogenin
     derivatives used to treat cognitive dysfunction comprises reduction of
     3-keto-5-beta-H-steroidal sapogenin using agent comprising a
     hindered organoborane or an organo-aluminium
     hydride
DC   B01
IN   GUNNING P J; TIFFIN P D
PA   (PHYT-N) PHYTOPHARM PLC; (PHYT-N) PHYTOTECH LTD
CYC  103
PIA  WO 2004037845   A1 20040506 (200435)* EN  41[0]
     AU 2003224308   A1 20040513 (200468)  EN
     EP 1558627      A1 20050803 (200551)  EN
     BR 2003015746   A  20050906 (200560)  PT
     TW 2004006215   A  20040501 (200571)  ZH
     US 20060041119  A1 20060223 (200615)  EN                          <--
     JP 2006507360   W  20060302 (200621)  JA  31
     CN 1723218      A  20060118 (200639)  ZH
     IN 2005MN00308  P3 20060505 (200659)  EN
     KR 2005090379   A  20050913 (200674)  KO
ADT  WO 2004037845 A1 WO 2003-GB1780 20030428; AU 2003224308 A1 AU
     2003-224308 20030428; BR 2003015746 A BR 2003-15746 20030428; CN 1723218 A
     CN 2003-824744 20030428; EP 1558627 A1 EP 2003-720733 20030428; TW
     2004006215 A TW 2003-109883 20030428; EP 1558627 A1 WO 2003-GB1780
     20030428; BR 2003015746 A WO 2003-GB1780 20030428; US
     20060041119 A1 WO 2003-GB1780 20030428; JP 2006507360 W
     WO 2003-GB1780 20030428; IN 2005MN00308 P3 WO 2003-GB1780
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20030428; JP 2006507360 W JP 2005-501542 20030428; IN 2005MN00308 P3 IN 2005-MN308 20050420; US 20060041119 A1 US 2005-531086 20050621; KR 2005090379 A WO 2003-GB1780 20030428; KR 2005090379 A KR 2005-707429 20050428

FDT AU 2003224308 A1 Based on WO 2004037845 A; EP 1558627 A1 Based on WO 2004037845 A; BR 2003015746 A Based on WO 2004037845 A; JP 2006507360 W Based on WO 2004037845 A; KR 2005090379 A Based on WO 2004037845 A

PRAI GB 2003-1505 20030122
GB 2002-25106 20021026

AB WO 2004037845 A1 UPAB: 20060121
NOVELTY - Preparation of 3-hydroxy-5beta-H-steroidal sapogenin (I) or its derivative comprises reduction of 3-keto-5beta-H-steroidal sapogenin using a reducing agent comprising a hindered organoborane or an organo-aluminium hydride. ACTIVITY - Nootropic.
No details of tests for nootorpic activity are given.
MECHANISM OF ACTION - None given in the source material.
USE - (I) are useful for the treatment of cognitive dysfunction.
ADVANTAGE - (I) are suitable for use incontact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response.

TECH
ORGANIC CHEMISTRY - Preferred Process: The reducing agent is a hindered organoborane reagent in which organic groups contain more than two carbon atoms and the sapogenin obtained is predominantly a 3beta-hydroxy, 5beta-H-sapogenin. The molar ratio of the predominant sapogenin obtained to the alternative 3-epimer, is at least 15:1 (preferably10:1).
Preferred Components: The hindered organoborane is lithium tri-sec-butylborohydride (preferred), potassium tri-sec-butylborohydride, sodium tri-sec-butylborohydride, lithium trisiamylborohydride, potassium trisiamylborohydride, potassium triphenylborohydride and lithium triphenylborohydride. The organo-aluminium hydride is lithium tri-tert-butoxyaluminohydride. Preparation is performed in an organic solvent such as tetrahydrofuran, toluene, 1,4-dioxan, 2-methyltetrahydrofuran (preferred), tert-butyl methyl ether and/or diethoxymethane. (I) is sarsasapogenin, episarsasapogenin, smilagenin, epismilagenin and its esters. The delta4, 3-keto steroidal sapogenin is diosgenone (diosgenone is obtained by oxidation of diosgenin). The desired sapogenin is formula (A).
R1, R2, R3, R4, R5, R6, R7, R8 and R9 = H, 1-4C alkyl, OH, or OR (where R is 6-12C aryl or 1-4C alkyl); or
R5+R6 = carbonyl or protected carbonyl group (the stereochemistry at carbon centre 3 can be either R or S); and
R10 = OH, O-linked sugar group or any organic ester group.

ABEX SPECIFIC COMPOUNDS - The use of sarsasapogenin, episarsasapogenin, smilagenin, epismilagenin is specifically claimed as (I).
EXAMPLE - No suitable example given.

L55 ANSWER 2 OF 10 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
AN 2003-902924 [82] WPIX Full-text
CR 2003-229198
DNC C2003-256428 [82]
TI Use of steroidal sapogenin derivatives in the preparation of compositions for treating e.g. non-cognitive neurodegeneration
DC B01; D13
IN GUNNING P; HU Y; ORSI A; REES D; XIA Z
PA (GUNN-I) GUNNING P; (HUYY-I) HU Y; (ORSI-I) ORSI A; (PHYT-N) PHYTOPHARM PLC; (REES-I) REES D; (XIAZ-I) XIA Z

CYC 103
PIA WO 2003082893 A2 20031009 (200382)* EN 30[6]
AU 2003229877 A1 20031013 (200435) EN
EP 1490071 A2 20041229 (200502) EN
BR 2003008788 A 20050111 (200512) PT
KR 2004093153 A 20041104 (200517) KO
NO 2004004468 A 20041223 (200520) NO
US 20050130948 A1 20050616 (200540) EN
JP 2005528370 W 20050922 (200563) JA 56
MX 2004009321 A1 20050201 (200564) ES
TW 2004000042 A 20040101 (200569) ZH
CN 1642558 A 20050720 (200575) ZH
NZ 535093 A 20060929 (200668) EN
ADT WO 2003082893 A2 WO 2003-GB1380 20030327; AU 2003229877 A1 AU 2003-229877 20030327; BR 2003008788 A BR 2003-8788 20030327; CN 1642558 A CN 2003-807188 20030327; EP 1490071 A2 EP 2003-722713 20030327; JP 2005528370 W JP 2003-580357 20030327; TW 2004000042 A TW 2003-106926 20030327; EP 1490071 A2 WO 2003-GB1380 20030327; BR 2003008788 A WO 2003-GB1380 20030327; NO 2004004468 A WO 2003-GB1380 20030327; US 20050130948 A1 WO 2003-GB1380 20030327; JP 2005528370 W WO 2003-GB1380 20030327; MX 2004009321 A1 WO 2003-GB1380 20030327; KR 2004093153 A KR 2004-714567 20040916; MX 2004009321 A1 MX 2004-9321 20040924; NO 2004004468 A NO 2004-4468 20041020; US 20050130948 A1 US 2005-507000 20050124; NZ 535093 A NZ 2003-535093 20030327; NZ 535093 A WO 2003-GB1380 20030327
FDT AU 2003229877 A1 Based on WO 2003082893 A; EP 1490071 A2 Based on WO 2003082893 A; BR 2003008788 A Based on WO 2003082893 A; JP 2005528370 W Based on WO 2003082893 A; MX 2004009321 A1 Based on WO 2003082893 A; NZ 535093 A Based on WO 2003082893 A
PRAI US 2002-368178P 20020328
AR 2002-101170 20020327
WO 2002-GB1578 20020328

AB WO 2003082893 A2 UPAB: 20060203
NOVELTY - Use of one or more steroidal sapogenin derivatives (I)-(III) in the preparation of compositions for treating non-cognitive neurodegeneration, non-cognitive neuromuscular degeneration, motor-sensory neurodegeneration, or receptor dysfunction or loss in the absence of cognitive, neural and neuromuscular impairment, is new.
DETAILED DESCRIPTION - Use of one or more steroidal sapogenin derivatives of formula (I)-(III), their stereoisomers, racemic mixtures, pro-drugs and/or salts (containing at least one X substituent; and the carbon atom at the 3-position, or in case of (II) and (III), the 3-position carbon and/or the 26-position carbon carries an O-sugar moiety in which sugar group is mono- to tri-saccharide) in the preparation of compositions for treating non-cognitive neurodegeneration, non-cognitive neuromuscular degeneration, motor-sensory neurodegeneration, or receptor dysfunction or loss in the absence of cognitive, neural and neuromuscular impairment, is new.
R1-R8, R10, R13, R18-R24, R26-R32, R34, R36, R37, R35a = T or =O; T = H, OH, halo, MeS, MeSO, MeSO2, N3, NH2, MeSO2NH, alkyl, absent or OR;
R = alkyl or acyl;
R9, R11, R12, R15-R17, R25, R35 = T; R14, R33 = T or alkyl;
R33a = T, =O or alkyl;
dotted line = optional double bond; and X = halo, MeS, MeSO, MeSO2, N3, NH2, MeSO2NH- or alkyl; provided that R25 in (III) is in beta-orientation. ACTIVITY - Neuroprotective; CNS-Gen; Muscular-Gen.; Nootropic; Antiparkinsonian; Antidepressant; Neuroleptic; Ophthalmological; Anticonvulsant; Hypertensive; Vulnerary; Cerebroprotective; Tranquilizer; Antiinflammatory; Immunomodulator; Antidiabetic; Vasotropic; Cardiant; Antiasthmatic.
The neuroprotective effect of sarsasapogenin (Ia) was evaluated in aged Sprague-Dawley rats by administration of (Ia) (18 mg/kg/day) through food for 2-3 months. The learning and memory abilities were assessed by using a Y-maze

apparatus and dopamine receptor density was assessed in the brain homogenate by the dual-site competitive ligand binding assay. The dopamine (D1/D2) receptor density was 157/200.6 fmol/mg protein in young rats (control 1); 129.2/153.8 fmol/mg protein in aged rats not receiving (Ia) (control 2); and 172/206.4 fmol/mg protein in aged rats receiving (Ia). In control 1/control 2/(Ia), muscarinic receptor density was 1000/875/1025 fmol/mg protein; and the learning and memory ability was 5.2/2/5.2 (no units), respectively. The results showed that (Ia) restored the dopamine and muscarinic receptors density as well as learning ability and memory in the aged rats by reversing the neuroimpairments.

MECHANISM OF ACTION - None given.

USE - For treating non-cognitive neurodegeneration; non-cognitive neuromuscular degeneration; motor-sensory neurodegeneration; and receptor dysfunction or loss in the absence of cognitive, neural and neuromuscular impairment (e.g. Parkinson's disease, postencephalitic Parkinsonism, depression, schizophrenia, muscular dystrophy (including facioscapulohumeral muscular dystrophy (FSH), Duchenne muscular dystrophy, Becker muscular dystrophy and Bruce's muscular dystrophy, Fuch's dystrophy, myotonic dystrophy, corneal dystrophy, reflex sympathetic dystrophy syndrome (RSDSA), neurovascular dystrophy), myasthenia gravis, Lambert Eaton disease, Huntington's disease, motor neuron diseases (including amyotrophic lateral sclerosis (ALS), multiple sclerosis), postural hypotension, traumatic neurodegeneration e.g. following stroke or following an accident (e.g. traumatic head injury or spinal cord injury), Batten's disease, Cockayne syndrome, Down syndrome, corticobasal ganglionic degeneration, multiple system atrophy, cerebral atrophy, olivopontocerebellar atrophy, dentatorubral atrophy, pallidoluysian atrophy, spinobulbar atrophy, optic neuritis, sclerosing pan-encephalitis (SSPE), attention deficit disorder, post-viral encephalitis, post-poliomyelitis syndrome, Fahr's syndrome, Joubert syndrome, Guillain-Barre syndrome, lissencephaly, Moyamoya disease, neuronal migration disorders, autistic syndrome, polyglutamine disease, Niemann-Pick disease, progressive multifocal leukoencephalopathy, pseudotumor cerebri, Refsum disease, Zellweger syndrome, supranuclear palsy, Friedreich's ataxia, spinocerebellar ataxia type 2, Rhett syndrome, Shy-Drager syndrome, tuberous sclerosis, Pick's disease, chronic fatigue syndrome, neuropathies including hereditary neuropathy, diabetic neuropathy and mitotic neuropathy, prion-based neurodegeneration (including Creutzfeldt-Jakob disease (CJD), variant CJD, new variant CJD, bovine spongiform encephalopathy (BSE), GSS, FFI, kuru and Alper's syndrome), Joseph's disease, acute disseminated encephalomyelitis, arachnoiditis, vascular lesions of the central nervous system, loss of extremity neuronal function, Charcot-Marie-Tooth disease, susceptibility to heart failure, asthma, or macular degeneration) in human and non-human animals (claimed).

ADVANTAGE - The compounds are strongly neuroprotective, stimulative of neurite outgrowth, and preventive of neurotoxicity. The compounds slow or reverse decrease in cholinergic and dopamine receptor density. The compounds reverse the receptor loss effects, simultaneously reversing the deterioration towards the normal or young state with protection. The compounds reverse the apoptotic effect in the non-neoplastic domain of cell life.

TECH

PHARMACEUTICALS - Preferred Components: The steroidal sapogenin derivative is present in a composition selected from pharmaceutical composition, foodstuff, food supplement or beverage; and is present with at least one additional active agent. The additional active agent is cholinesterase inhibitor, dopamine agonist, COMT inhibitor, MAO-B inhibitor, anti-cholinergic, acetylcholine agonist, serotonin agonist, alpha-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) receptor agonist, gamma-aminobutyric acid (GABA) receptor agonist, N-methyl-D-aspartate (NMDA) receptor agonist, beta-adrenoceptor agonist, digoxin, dobutamine, anti-inflammatory, neurotrophic factor, statin,

adenosine A2a receptor antagonist, aldose reductase inhibitor, immunomodulator, cannabinoid agonist, interferon beta or tricyclic anti-depressant.

ABEX ADMINISTRATION - Administration of (I)-(III) is more than 0.1 or 0.3 (preferably 1-10) mg/kg/day orally, by sprays, by inhalation, as suppositories or by injection (including liposome preparation).
SPECIFIC COMPOUNDS - Use of 148 compounds (I)-(III) is specifically claimed, e.g. sarsasapogenin (Ia).
EXAMPLE - No relevant example given.

L55 ANSWER 3 OF 10 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
AN 2003-765551 [72] WPIX Full-text
CR 2001-541229; 1999-496233; 2000-604069; 2001-343159
DNC C2003-210173 [72]
TI Treating and preventing cognitive dysfunction e.g. Alzheimer's disease, Parkinson's disease and autism comprises administering 5-hydroxysapogenin derivative
DC B01; D13
IN BARRACLOUGH P; GUNNING P; HANSON J; HU Y; REES D; XIA Z
PA (BARR-I) BARRACLOUGH P; (GUNN-I) GUNNING P; (HANS-I) HANSON J; (HUYY-I) HU Y; (REES-I) REES D; (XIAZ-I) XIA Z
CYC 1
PIA US 20030100542 A1 20030529 (200372)* EN 14[2]
ADT US 20030100542 A1 CIP of WO 2000-GB3750 20000929; US 20030100542 A1 US 2002-108737 20020328
PRAI US 2002-108737 20020328
WO 2000-GB3750 20000929
AB US 20030100542 A1 UPAB: 20050601
NOVELTY - Treating and preventing cognitive dysfunction comprises administering a 5-hydroxysapogenin derivative (I).
DETAILED DESCRIPTION - Treating and preventing cognitive dysfunction comprises administering a 5-hydroxysapogenin derivative of formula (IA), its stereoisomers, racemic mixtures, prodrugs or salts.
R1-R8, R10 = H, OH, O or OR; R = alkyl, acyl or carbamoyl (all optionally substituted), or alkoxycarbonyl;
R9, R11-R13 = H, OH or OR, and R14 = optionally substituted alkyl. The stereochemistry at 5C is (R) or (S). When (I) is in prodrug form, at least one of the above groups carries a group hydrolyzed off in vivo to form (I).
INDEPENDENT CLAIMS are also included for: (1) a pharmaceutical composition comprises (I), its pro-drug or salt in association with at least one carrier, diluent or excipient, and (2) new compounds (I), provided that when R1, R2, R4, R9 and R10 are H or OH, R6, R7 and R11-R13 are H, R5 and R8 are H, OH or O, R14 is methyl or =CH2 and a is single bond, then R3 is not OH, OCOCH3, OCOC15H31 or O.
ACTIVITY - Nootropic; Neuroprotective; Antiparkinsonian; Hypotensive; Muscular-Gen.; CNS-Gen; Immunomodulator.
MECHANISM OF ACTION - Muscarinic receptor agonist; Nicotinic receptor agonist; Dopamine receptor agonist. In a test for evaluating the effect of anzurogenin D (Ia) on the expression of muscarinic (M2) receptors on Chinese hamster ovary (CHO) cells transfected with DNA for the M2 receptor, results showed that the effect of (Ia) on the expression of M2 receptors was 22%.
USE - Used for treating or preventing age-related cognition, Alzheimer's disease, senile dementia of the Alzheimer's type, Parkinson's disease, Lewy body dementia, postural hypotension, autism, chronic fatigue syndrome, Myasthenia Gravis, Lambert Eaton disease and problems associated with aging, and for treating a condition mediated by the presence of neurofibrillary tangles and beta-amyloid plaques (all claimed).
ADVANTAGE - (I) Selectively increases muscarinic receptor number, which increases synaptic transmission. (I) Increases stimulation of protein kinase C (PKC) with consequential increase in alpha-secretory activity, which reduces

the production of beta-amyloid, plaque formation and neuronal loss. (I) Also increases amyloid precursor proteins-alpha (APPsalpha), which improves cerebral function.

TECH PHARMACEUTICALS - Preferred Composition: The composition comprises (I) in the form of an extract derived from a plant of Smilax, Asparagus, Anemarrhena, Yucca or Agave.
ORGANIC CHEMISTRY - Preparation: (I) Are prepared by known methods e.g. described by R. C. Larock in Comprehensive Organic Transformations, VCH publishers, 1989.

ABEX ADMINISTRATION - Administration is in the form of a foodstuff, food supplement or beverage (claimed). No dosage is given.
EXAMPLE - None given.

L55 ANSWER 4 OF 10 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
AN 2003-229198 [22] WPIX Full-text
CR 2003-902924
DNC C2003-058766 [22]
TI New use of sapogenin derivatives in the preparation of composition for the treatment or prevention of non-cognitive neurodegeneration, non-cognitive neuromuscular degeneration e.g. Alzheimer's disease
DC B01
IN BARRACLOUGH P; GUNNING P; HANSON J; HU Y; REES D; XIA Z
PA (BARR-I) BARRACLOUGH P; (GUNN-I) GUNNING P; (HANS-I) HANSON J; (HUYY-I) HU Y; (PHYT-N) PHYTOPHARM LTD; (PHYT-N) PHYTOTECH LTD; (REES-I) REES D; (XIAZ-I) XIA Z; (PHYT-N) PHYTOPHARM PLC
CYC 99
PIA WO 2002079221 A2 20021010 (200322)* EN 52[5] <--
NO 2003004364 A 20031128 (200407) NO
EP 1383787 A2 20040128 (200409) EN
BR 2002008533 A 20040420 (200428) PT
AU 2002242894 A1 20021015 (200432) EN <--
CZ 2003002620 A3 20040414 (200435) CS
KR 2004007479 A 20040124 (200435) KO
US 20040147495 A1 20040729 (200450) EN
JP 2004525945 W 20040826 (200456) JA 98
MX 2003008800 A1 20041201 (200561) ES
IN 2003CN01687 P4 20051125 (200604) EN
NZ 529136 A 20051223 (200605) EN
CN 1678325 A 20051005 (200606) ZH
NZ 540712 A 20070126 (200711) EN
ADT WO 2002079221 A2 WO 2002-GB1578 20020328; AU 2002242894 A1 AU 2002-242894 20020328; BR 2002008533 A BR 2002-8533 20020328; CN 1678325 A CN 2002-807427 20020328; EP 1383787 A2 EP 2002-708534 20020328; JP 2004525945 W JP 2002-577845 20020328; NZ 529136 A NZ 2002-529136 20020328; NO 2003004364 A WO 2002-GB1578 20020328; EP 1383787 A2 WO 2002-GB1578 20020328; BR 2002008533 A WO 2002-GB1578 20020328; CZ 2003002620 A3 WO 2002-GB1578 20020328; US 20040147495 A1 WO 2002-GB1578 20020328; JP 2004525945 W WO 2002-GB1578 20020328; MX 2003008800 A1 WO 2002-GB1578 20020328; IN 2003CN01687 P4 WO 2002-GB1578 20020328; NZ 529136 A WO 2002-GB1578 20020328; CZ 2003002620 A3 CZ 2003-2620 20020328; MX 2003008800 A1 MX 2003-8800 20030926; KR 2004007479 A KR 2003-712755 20030929; NO 2003004364 A NO 2003-4364 20030929; IN 2003CN01687 P4 IN 2003-CN1687 20031023; US 20040147495 A1 US 2004-472892 20040304; NZ 540712 A Div Ex NZ 2002-280302 20020328; NZ 540712 A NZ 2002-540712 20020328
FDT EP 1383787 A2 Based on WO 2002079221 A; BR 2002008533 A Based on

WO 2002079221 A; AU 2002242894 A1 Based on WO 2002079221 A; CZ 2003002620 A3 Based on WO 2002079221 A; JP 2004525945 W Based on WO 2002079221 A; MX 2003008800 A1 Based on WO 2002079221 A; NZ 529136 A Based on WO 2002079221 A; NZ 540712 A Div ex NZ 529136 A

PRAI GB 2001-7822 20010328
AR 2002-101170 20020327

AB WO 2002079221 A2 UPAB: 20060119

NOVELTY - New use of sapogenin derivatives in the preparation of composition for the treatment or prevention of non-cognitive neurodegeneration, non-cognitive neuromuscular degeneration or receptor loss in the absence of cognitive, neural and neuromuscular impairment in human and non-human animals.

DETAILED DESCRIPTION - New use for sapogenin derivatives of formula (II), their stereoisomers, racemic mixtures or their salts, in the preparation of composition for the treatment or prevention of: (1) non-cognitive neurodegeneration; (2) non-cognitive neuromuscular degeneration; or (3) receptor loss in the absence of cognitive, neural and neuromuscular impairment in human and non-human animals suffering from or susceptible to it.

R = H, alkoxycarbonyl or alkylcarbonyl (where the alkyl is optionally substituted by aryl, amino, mono- or di-alkyl amino or carboxylic acid residue).

INDEPENDENT CLAIMS are also included for: (1) compounds of formula (II) (where R is alkoxycarbonyl or alkylcarbonyl (where the alkyl is optionally substituted by aryl, amino, alkoxycarbonylamino, mono-alkylamino, di-alkylamino, N-alkyl, N-alkoxycarbonylamino or carboxylic acid residue)) with the provision that:

(a) when the stereochemistry of 3C is alpha and of 25C is S simultaneously, R is not unsubstituted acetyl; (b) when the stereochemistry of 3C is S(beta) and of 25C is R simultaneously, R is not unsubstituted ethoxycarbonyl; (c) when the stereochemistry of 3C is S(beta) and of 25C is S; or the stereochemistry of 3C is R(alpha) or S(beta) and of 25C is R; then R is not succinyl; and (d) when the stereochemistry of 25C is R and the stereochemistry of 3C is S(beta), R is not propionyl, butyryl, valeryl, isovaleryl, (iso)caproyl, diethylacetyl, octanoyl, decanoyl, lauryl, myristyl, palmityl, stearyl, benzoyl, phenylacetyl, phenylpropionate, cinnamate, para-nitrobenzoate, 3,5-dinitrobenzoate, para-chlorobenzoate, 2,4-dichlorobenzoyl, para-bromobenzoyl, meta-bromobenzoyl, para-methoxybenzoyl, furoyl or phthalyl; (2) a method of synthesizing compounds of formula (II) (other than those with R is H);

(3) a method of synthesizing a steroidal sapogenin derivative comprising treating a steroidal sapogenin with ethylchloroformate in the presence of a base to form the 3-ethoxycarbonyl derivative;

(4) a method of synthesizing a steroidal sapogenin derivative (B) comprising treating a selected steroidal sapogenin with ethylchloroformate or related reagent in the presence of a base; (5) a method of synthesizing episarsasapogenin cathylate from episarsasapogenin comprising treating episarsasapogenin with ethylchloroformate or related reagent and base or succinic anhydride or related reagent and a base; and (6) a composition (A) comprising (II) with the provisions (a) - (d).

ACTIVITY - Nootropic; Neuroprotective; Antiparkinsonian; Anticonvulsant; Hypertensive; Antiasthmatic; Cardiant; Virucide.

MECHANISM OF ACTION - Receptor regulators; Muscarinic receptor stimulator. Sarsasapogenin was tested for brain muscarinic receptor density in Alzheimer's disease model. Three months old, Sprague Dawley rats were divided into two groups. Injection of amyloid beta1-40 and ibotenic acid was accomplished. The dose for each rat was amyloid beta1-40 (4 microg) and ibotenic acid (1 microg) in saline (1 microl). The injection was completed in 20 minutes and the needle was withdrawn 10 minutes later. One group of rats was given sarsasapogenin cathylate (18 mg/kg/day) (test) as stable suspension in CMC-Na once daily through gastric tube. The other group (control) was given same volume of CMC-Na (i.e. normal saline) once daily. The drugs were administered to the rats for 2 months, starting 20 days before operation. The brain samples were

homogenized, centrifuged and the pellets of the centrifugation were re-homogenized and used for measurement. The effect of test on memory was assessed using step-through test. The experiment was carried out on rats on two consecutive days. On the first day, the rats were adapted in the box for first 3 minutes and then put in light room with its back toward the hole and the copper rods of the dark room were charged for 5 minutes. On second day the rats were tested. The muscarinic receptor density in Alzheimer's model brain in the test/control was (fmol/mg/protein): 916+/-158/859+/-101.
The results showed that the muscarinic receptor density in Alzheimer's model brain in the test was lower than in the control. The test showed significant elevation in brain muscarinic receptor density. The results showed that the test normalized receptor number i.e. they restored receptor number to normal levels.
USE - (II) are used in the manufacture of a composition or medicament for the treatment or prevention of non-cognitive neurodegeneration, non-cognitive neuromuscular degeneration and receptor loss in the absence of cognitive, neural and neuromuscular impairment in human or non-human animals; for treating or preventing cognitive dysfunction e.g. Alzheimer's disease, senile dementia of the Alzheimer's type, SDAT, AAMI, Lewi body dementia and autism in human or non-human animals; in the treatment of disorders such as Parkinson's disease, muscular dystrophy including facioscapulohumeral muscular dystrophy (FSH), Duchenne muscular dystrophy, Becker muscular dystrophy and Bruce's muscular dystrophy, Fuchs' dystrophy, myotonic dystrophy, corneal dystrophy, reflex sympathetic dystrophy syndrome (RSDSA), epilepsy, disease and problems associated with ageing, neurovascular dystrophy, myasthenia gravis, Lambert Eaton disease, Huntington's disease, amyotrophic lateral sclerosis, multiple sclerosis, postural hypotension, chronic fatigue syndrome, asthma, susceptibility to heart failure, and macular degeneration; in age-related cognitive dysfunction. Also, (II) are used as a foodstuff, food product, food supplement or beverage (claimed); or in the treatment of viral diseases.
ADVANTAGE - (II) increases the receptor number or turnover and enhances the function of receptors in a human or non-human animals. (II) prevents or reverses the loss of muscarinic receptors or dopamine receptors in the brain. (II) reverses the loss of, and/or increases muscarinic receptor number leading to increased synaptic transmission. The reversal of the loss of and/or increase in the number of nicotinic receptors, which lies upstream of the synaptic cleft leads to increase in the reversal of loss of acetylcholine release into the synaptic cleft, thus increasing muscarinic receptor activation and amplifying the overall effect. (II) increases receptor numbers leading to reduced production of beta-amyloid and consequent reduction of plaque formation and neuronal loss. (II) increases amyloid precursor protein (APP)s-alpha and improves cerebral function by improving short and long term memory.

TECH

ORGANIC CHEMISTRY - Preferred Components: (II) has 25C methyl group in R or S configuration.
The compound L-R' is carboxylic acid, an anhydride or an acyl halide.
The base is dry pyridine dissolved in dry dichloromethane.
Preparation: (II) is prepared (other than those with R is H) by reacting (II) (where R is H) with a compound of formula L-R' under nucleophilic substitution conditions.
R' = alkoxycarbonyl or alkylcarbonyl (where the alkyl is optionally substituted by aryl, amino, mono-alkylamino, di-alkylamino, or carboxylic acid residue.
(B) is epismilagenin cathylate (synthesized from epismilagenin), and sarsasapogenin cathylate (synthesized from sarsasapogenin).
BIOLOGY - Preferred Extract: The sarsasapogenin is in the form of a plant extract or dry powdered, plant material, derived from a plant e.g. Smilax Asparagus, Aanemarrrhena, Dioscorea, Yuccaa or Agave.

FOOD - Preferred Composition: (A) is a foodstuff, food supplement or beverage.

ABEX DEFINITIONS - Preferred Definitions: - R = lower alkoxycarbonyl or lower alkylcarbonyl optionally substituted by terminal carboxylic acid residue. ADMINISTRATION - (II) is administered in a dosage of 1 - 25 (preferably 1 - 10) mg/kg by inhalation, as spray, as liquid or liposome preparation. SPECIFIC COMPOUNDS - The use of 40 compounds of formula (II) are specifically claimed, e.g. sarsasapogenin.

L55 ANSWER 5 OF 10 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
AN 2001-541229 [60] WPIX Full-text
CR 1999-496233; 2000-604069; 2001-343159; 2003-765551
DNC C2001-161463 [60]
TI New sapogenin derivatives, useful for treating e.g. cognitive dysfunction, Parkinson's disease, postural hypotension, autism, chronic fatigue syndrome and ageing problems by increasing muscarinic receptor number and function
DC B01
IN BARRACLOUGH P; GUNNING P; HANSON J; HU Y; REES D; TOBIN A; XIA Z
PA (PHYT-N) PHYTOPHARM PLC
CYC 93
PIA WO 2001023408 A1 20010405 (200160)* EN 31[2] <--
AU 2000075387 A 20010430 (200160) EN <--
BR 2000014372 A 20020625 (200251) PT <--
EP 1224207 A1 20020724 (200256) EN <--
CN 1377366 A 20021030 (200314) ZH
JP 2003525869 W 20030902 (200358) JA 36
MX 2002003307 A1 20021001 (200370) ES <--
EP 1224207 B1 20060215 (200614) EN
DE 60026046 E 20060420 (200628) DE
US 20060165757 A1 20060727 (200650) EN
ES 2257321 T3 20060801 (200652) ES
DE 60026046 T2 20061005 (200665) DE
ADT WO 2001023408 A1 WO 2000-GB3750 20000929; US 20060165757 A1 CIP of WO 1999-GB951 19990326; AU 2000075387 A AU 2000-75387 20000929; BR 2000014372 A BR 2000-14372 20000929; CN 1377366 A CN 2000-813604 20000929; DE 60026046 E DE 2000-626046 20000929; EP 1224207 A1 EP 2000-964452 20000929; EP 1224207 B1 EP 2000-964452 20000929; DE 60026046 E EP 2000-964452 20000929; ES 2257321 T3 EP 2000-964452 20000929; BR 2000014372 A WO 2000-GB3750 20000929; EP 1224207 A1 WO 2000-GB3750 20000929; JP 2003525869 W WO 2000-GB3750 20000929; MX 2002003307 A1 WO 2000-GB3750 20000929; EP 1224207 B1 WO 2000-GB3750 20000929; DE 60026046 E WO 2000-GB3750 20000929; US 20060165757 A1 CIP of WO 2000-GB3750 20000929; JP 2003525869 W JP 2001-526558 20000929; MX 2002003307 A1 MX 2002-3307 20020327; US 20060165757 A1 Cont of US 2002-108737 20020328; US 20060165757 A1 US 2006-346046 20060202; DE 60026046 T2 DE 2000-626046 20000929; DE 60026046 T2 EP 2000-964452 20000929; DE 60026046 T2 WO 2000-GB3750 20000929
FDT DE 60026046 E Based on EP 1224207 A; ES 2257321 T3 Based on EP 1224207 A; AU 2000075387 A Based on WO 2001023408 A; BR 2000014372 A Based on WO 2001023408 A; EP 1224207 A1 Based on WO 2001023408 A; JP 2003525869 W Based on WO 2001023408 A; MX 2002003307 A1 Based on WO 2001023408 A; EP 1224207 B1 Based on WO 2001023408 A; DE 60026046 E Based on WO 2001023408 A; DE 60026046 T2 Based on EP 1224207 A; DE 60026046 T2 Based on WO 2001023408 A
PRAI GB 1999-23078 19990929
AB WO 2001023408 A1 UPAB: 20050526

NOVELTY - Sapogenin derivatives (I) and their stereoisomers and racemic mixtures, pro-drugs and salts are new.
DETAILED DESCRIPTION - Sapogenin derivatives of formula (I) and their stereoisomers and racemic mixtures, pro-drugs and salts are new.
R1 - R8, R10 = H, OH, =O, or OR; R = optionally substituted alkyl, acyl, or carbamoyl, or alkoxycarbonyl;
R9, R11 - R13 = H, OH, or OR; R14 = optionally substituted alkyl; and dashed line = optional double bond; the stereochemistry at C5 can be either R or S.
INDEPENDENT CLAIMS are also included for: (1) the use of (I) in the manufacture of a medicament for increasing the muscarinic receptor number or enhancing the function of muscarinic receptors;
(2) a pharmaceutical composition having cognitive function enhancing properties in the form of an extract derived from a plant of the genus Smilax, Asparagus, Anemarrhena, Yucca, or Agave; (3) a non-therapeutic method of enhancing cognitive function; and (4) the use of (I) in a food product or beverage to enhance cognitive function.
ACTIVITY - Nootropic; Neuroprotective; Antiparkinsonian; Hypertensive.
MECHANISM OF ACTION - Increase muscarinic receptor number and function.
The effect of sapogenin derivatives on muscarinic receptor density in Chinese hamster ovary (CHO) cells expressing recombinant human muscarinic receptors was studied. CHO cells expressing high levels of receptor (approximately 2.2 moles receptor/mg protein) were cultured in flasks (150ml) for 24 hours before the start of the experiment. Vehicle (DMSO) and sapogenin derivative (at 1 and 10microM) were added to the medium for 48 hours. The culture medium was discarded, the cells scraped off and resuspended in Hanks solution, centrifuged and m-receptor levels determined by incubating with (3H)-QNB for 30 minutes followed by liquid scintillation counting. Protein levels were determined by a micro Lowry method. The results showed that over the culturing period treatment with sapogenin derivatives prevents the decrease in muscarinic receptor number in a concentration-dependent manner.
USE - The compounds can be used for increasing the muscarinic receptor number or enhancing the function of muscarinic receptors in a human or non-human animal (claimed). They can be used for treating cognitive dysfunction, Alzheimer's disease, senile dementia of the Alzheimer's type, Parkinson's disease, Lewi body dementia, postural hypotension, autism, chronic fatigue syndrome, myasthenia gravis, Lambert Eaton disease, diseases and problems associated with Gulf War syndrome, occupational exposure to organophosphorus compounds and problems associated with ageing (claimed). They can also be used to enhance cognitive function in a patient suffering from age-related cognitive dysfunction (claimed). They can be used to treat a condition characterized by the presence of neurofibrillary tangles and/or beta-amyloid plaques (claimed).

TECH ORGANIC CHEMISTRY - Preparation: (I) can be prepared by synthetic methods from unsubstituted sapogenins. The reactions may involve the substitution of one OH-group by the functional radical desired, smilagenin and epismilagenin are preferred as starting products.

ABEX DEFINITIONS - Preferred definitions: - R1, R2, R4, R6, R7, R8, R10, R11, R9, R12, R13 = H; - R3, R5 = OH or OCOCH3, or =O; and - R14 = CH3.
ADMINISTRATION - None given.
SPECIFIC COMPOUNDS - A preferred compound, Anzurogenin D of formula (Ia) is disclosed.

L55 ANSWER 6 OF 10 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
AN 2001-475962 [51] WPIX Full-text
DNC C2001-142769 [51]
TI New sapogenin derivatives which increase muscarinic receptors in brain, useful for treating e.g. Alzheimer's or Parkinson's disease, dementia, autism, chronic fatigue syndrome, exposure to organophosphorus

compounds and aging problems

DC B01

IN BARRACLOUGH P; GUNNING P; HANSON J; HU Y; REES D; XIA Z

PA (PHYT-N) PHYTOPHARM PLC

CYC 93

PIA WO 2001049703 A2 20010712 (200151)* EN 44[1] <--
AU 2001023862 A 20010716 (200169) EN <--
EP 1246835 A2 20021009 (200267) EN <--
JP 2003519624 W 20030624 (200341) JA 67
US 20030158161 A1 20030821 (200356) EN
MX 2002006720 A1 20021001 (200370) ES <--
CN 1452630 A 20031029 (200409) ZH
BR 2001007691 A 20050322 (200522) PT
CN 1215080 C 20050817 (200647) ZH

ADT WO 2001049703 A2 WO 2001-GB48 20010108; AU 2001023862 A AU 2001-23862 20010108; BR 2001007691 A BR 2001-7691 20010108; CN 1452630 A CN 2001-803540 20010108; EP 1246835 A2 EP 2001-900185 20010108; JP 2003519624 W JP 2001-550243 20010108 ; EP 1246835 A2 WO 2001-GB48 20010108; JP 2003519624 W WO 2001-GB48 20010108; US 20030158161 A1 CIP of WO 2001-GB48 20010108; MX 2002006720 A1 WO 2001-GB48 20010108; BR 2001007691 A WO 2001-GB48 20010108; US 20030158161 A1 US 2002-189024 20020703; MX 2002006720 A1 MX 2002-6720 20020705 ; CN 1215080 C CN 2001-803540 20010108

FDT AU 2001023862 A Based on WO 2001049703 A; EP 1246835 A2 Based on WO 2001049703 A; MX 2002006720 A1 Based on WO 2001049703 A; BR 2001007691 A Based on WO 2001049703 A; JP 2003519624 W Based on WO 2001049703 A

PRAI GB 2000-228 20000106

AB WO 2001049703 A2 UPAB: 20050902

NOVELTY - Sapogenin derivatives with at least one X group comprising halo, Me-S-, Me-SO-, Me-SO2-, N3-, NH2-, MeSO2NH- or alkyl, are new.

ACTIVITY - Neuroprotective; nootropic; antiparkinsonian, hypertensive.

MECHANISM OF ACTION - (I) Increase the number of muscarinic M2 receptors in the brain.

A test is described, but no results are given.

USE - Used in the regulation of cellular activity or for the treatment of a condition characterized by a deficiency in postsynaptic membrane-bound receptor number or function (claimed). (I) regulate receptors and/or increase the number of M2 receptors in the brain. (I) Are used for treating Alzheimer's disease or a senile dementia of the Alzheimer's type, Parkinson's disease, Lewi body dementia, postural hypotension, autism, chronic fatigue syndrome, myasthenia gravis, Lambert Eaton disease, diseases and problems associated with Gulf War syndrome, occupational exposure to organophosphorus compounds and problems associated with aging.

(I) Are also be used to treat a condition characterized by the presence of neurofibrillary tangles and/or beta-amyloid plaques, or to enhance cognitive function e.g. in a patient suffering from age-related dysfunction.

TECH

ORGANIC CHEMISTRY - Preferred compounds: The sapogenin compounds are of formula (I), their stereoisomers, racemic mixtures, prodrugs or salts.

R1-R8, R10, R13, R21-R24, R26-R32, R34, R35 = H, OH, =O or OR;

R = alkyl, acyl or absent;

R9, R11, R12, R15-R17, R25 = H, OH or OR;

R33, R14 = H, alkyl, OH, =O or R, and

at least one of R1-R18, R21-R35 = X.

Preparation: (I) Are prepared from starting materials comprising unsubstituted sapogenins obtained from Smilax, Asparagus, Anemarrhena, Yucca or Agave.

ABEX ADMINISTRATION - (I) Are used in food products or beverages. SPECIFIC COMPOUNDS - 6 Compounds (I) are specifically claimed e.g: - 3beta-fluoro-5beta, 20alpha,22alpha,25R-spirostane (Ia). EXAMPLE - Methylsulfonyl chloride (1.83 g) was added to a solution of smilagenin (5.0 g) in dry pyridine (40 ml). The mixture was heated on a steam bath for 10 minutes, allowed to stand overnight at room temperature and then poured onto ice-water (80 ml). Trituration gave an off-white solid, which was removed by filtration and washed with water. This material was dried in a vacuum desiccator over CaCl2 to give 5.70 g of crude product. - A sample (1.0 g) was recrystallized from acetone (2 x) to give 340 mg of 3beta-methylsulfonyloxy-5beta,20alpha,22alpha,25R-spirostane (Ib).

L55 ANSWER 7 OF 10 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
AN 2001-397532 [42] WPIX Full-text
DNC C2001-120809 [42]
TI New sapogenin derivatives, useful for treating e.g. cognitive dysfunction, Alzheimer's disease, postural hypotension, autism, chronic fatigue syndrome and ageing problems by increasing muscarinic receptor number and function
DC B01
IN BARRACLOUGH P; GUNNING P; HANSON J; HU Y; REES D; TOBIN A; XIA Z
PA (BARR-I) BARRACLOUGH P; (GUNN-I) GUNNING P; (HANS-I) HANSON J; (HUYY-I) HU Y; (PHYT-N) PHYTOPHARM PLC; (REES-I) REES D; (XIAZ-I) XIA Z
CYC 91

PIA	WO 2001023407	A1	20010405 (200142)*	EN	32[2]	<--
	AU 2000075382	A	20010430 (200142)	EN		<--
	BR 2000014355	A	20020716 (200255)	PT		<--
	EP 1224206	A1	20020724 (200256)	EN		<--
	US 20020183294	A1	20021205 (200301)	EN		
	CN 1377367	A	20021030 (200314)	ZH		
	JP 2003510333	W	20030318 (200321)	JA	48	
	MX 2002003306	A1	20021001 (200370)	ES		<--
	EP 1224206	B1	20040922 (200462)	EN		
	DE 60014136	E	20041028 (200471)	DE		
	ES 2228608	T3	20050416 (200528)	ES		
	EP 1548025	A2	20050629 (200543)	EN		
	DE 60014136	T2	20051006 (200566)	DE		

ADT WO 2001023407 A1 WO 2000-GB3745 20000929; AU 2000075382 A AU 2000-75382 20000929; BR 2000014355 A BR 2000-14355 20000929; CN 1377367 A CN 2000-813605 20000929; DE 60014136 E DE 2000-60014136 20000929; DE 60014136 T2 DE 2000-60014136 20000929; EP 1224206 A1 EP 2000-964447 20000929; EP 1224206 B1 EP 2000-964447 20000929; DE 60014136 E EP 2000-964447 20000929; ES 2228608 T3 EP 2000-964447 20000929; EP 1548025 A2 Div Ex EP 2000-964447 20000929; DE 60014136 T2 EP 2000-964447 20000929; BR 2000014355 A WO 2000-GB3745 20000929; EP 1224206 A1 WO 2000-GB3745 20000929; US 20020183294 A1 CIP of WO 2000-GB3745 20000929; JP 2003510333 W WO 2000-GB3745 20000929; MX 2002003306 A1 WO 2000-GB3745 20000929; EP 1224206 B1 WO 2000-GB3745 20000929; DE 60014136 E WO 2000-GB3745 20000929; DE 60014136 T2 WO 2000-GB3745 20000929; JP 2003510333 W JP 2001-526557 20000929; MX 2002003306 A1 MX 2002-3306 20020327; US 20020183294 A1 US 2002-109204 20020328; EP 1548025 A2 EP 2004-21601 20000929

FDT DE 60014136 E Based on EP 1224206 A; ES 2228608 T3 Based on EP 1224206 A; EP 1548025 A2 Div ex EP 1224206 A; DE 60014136 T2 Based on EP 1224206 A; AU 2000075382 A Based on WO 2001023407 A; BR 2000014355 A Based on WO

2001023407 A; EP 1224206 A1 Based on WO 2001023407 A; JP 2003510333 W Based on WO 2001023407 A; MX 2002003306 A1 Based on WO 2001023407 A; EP 1224206 B1 Based on WO 2001023407 A; DE 60014136 E Based on WO 2001023407 A; DE 60014136 T2 Based on WO 2001023407 A

PRAI GB 1999-23077 19990929

AB WO 2001023407 A1 UPAB: 20060117
NOVELTY - Sapogenin derivatives (I) and (II) and their stereoisomers and racemic mixtures, pro-drugs and salts are new.
DETAILED DESCRIPTION - Sapogenin derivatives of formula (I) and (II) and their stereoisomers and racemic mixtures, pro-drugs and salts are new.
R1 - R8, R10, R17 = H, OH, =O, or OR; R = optionally substituted alkyl, acyl, or carbamoyl, or alkoxycarbonyl;
R9, R11 - R13 = H, OH, or OR; R14 = optionally substituted alkyl; R15, R16 = H, or optionally substituted alkyl or acyl; dashed line = optional double bond; the H at C5 may be either alpha or beta. INDEPENDENT CLAIMS are also included for: (1) the use (I) or (II) for the manufacture of a medicament for increasing the muscarinic receptor number of enhancing the function of muscarinic receptor;
(2) a pharmaceutical composition with cognitive function enhancing properties in the form of an extract derived from a plant of the genus Smilax, Asparagus, Anemarrhena, Yucca or Agave; (3) a non-therapeutic method of enhancing cognitive function; and (4) the use of (I) or (II) in a food product or beverage to enhance cognitive function.
ACTIVITY - Nootropic; Neuroprotective; Antiparkinsonian; Hypertensive.
MECHANISM OF ACTION - Increase muscarinic receptor number and function.
The effect of sapogenin derivatives on muscarinic receptor density in Chinese hamster ovary (CHO) cells expressing recombinant human muscarinic receptors was studied. CHO cells expressing high levels of receptor (approximately 2.2 moles receptor/mg protein) were cultured in flasks (150ml) for 24 hours before the start of the experiment. Vehicle (DMSO) and sapogenin derivative (at 1 and 10microM) were added to the medium for 48 hours. The culture medium was discarded, the cells scraped off and resuspended in Hanks solution, centrifuged and m-receptor levels determined by incubating with (3H)-QNB for 30 minutes followed by liquid scintillation counting. Protein levels were determined by a micro Lowry method. The results showed that over the culturing period treatment with sapogenin derivatives prevents the decrease in muscarinic receptor number in a concentration-dependent manner.
USE - The compounds can be used for increasing the muscarinic receptor number or enhancing the function of muscarinic receptors in a human or non-human animal (claimed). They can be used for treating cognitive dysfunction, Alzheimer's disease, senile dementia of the Alzheimer's type, Parkinson's disease, Lewi body dementia, postural hypotension, autism, chronic fatigue syndrome, myasthenia gravis, Lambert Eaton disease, diseases and problems associated with Gulf War syndrome, occupational exposure to organophosphorus compounds and problems associated with ageing (claimed). They can also be used to enhance cognitive function in a patient suffering from age-related cognitive dysfunction (claimed). They can be used to treat a condition characterized by the presence of neurofibrillary tangles and/or beta-amyloid plaques (claimed).

TECH ORGANIC CHEMISTRY - (I) and (II) can be prepared by synthetic methods from unsubstituted sapogenins. The reactions may involve the substitution of one OH-group by the functional radical desired, smilagenin and epismilagenin are preferred as starting products.

ABEX ADMINISTRATION - None given
SPECIFIC COMPOUNDS - A preferred compound, E/F-Seco-tigogenin of formula (Ia) is disclosed.

L55 ANSWER 8 OF 10 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN

AN 2001-343159 [36] WPIX Full-text
CR 1999-496233; 2000-604069; 2001-541229; 2003-765551
DNC C2001-106195 [36]
TI New Bapogenin derivatives, useful for treating e.g. cognitive dysfunction, Alzheimer's disease, Parkinson's disease, autism, chronic fatigue syndrome, and ageing problems by increasing muscarinic receptor number and function
DC B01; B04
IN BARRACLOUGH P; GUNNING P; HANSON J; HU Y; REES D; TOBIN A; XIA Z
PA (BARR-I) BARRACLOUGH P; (GUNN-I) GUNNING P; (HANS-I) HANSON J; (HUYY-I) HU Y; (PHYT-N) PHYTOPHARM PLC; (REES-I) REES D; (XIAZ-I) XIA Z
CYC 93

PIA	WO 2001023406	A1	20010405	(200136)*	EN 43[4]	<--
	AU 2000075375	A	20010430	(200142)	EN	<--
	NO 2002001541	A	20020528	(200248)	NO	<--
	BR 2000014381	A	20020625	(200251)	PT	<--
	EP 1224205	A1	20020724	(200256)	EN	<--
	US 20030004147	A1	20030102	(200305)	EN	
	CZ 2002001114	A3	20021211	(200309)	CS	
	CN 1377368	A	20021030	(200314)	ZH	
	JP 2003510332	W	20030318	(200321)	JA 50	
	KR 2002092914	A	20021212	(200328)	KO	
	ZA 2002002382	A	20030923	(200368)	EN 61	
	MX 2002003305	A1	20021001	(200370)	ES	<--
	NZ 518596	A	20040730	(200454)	EN	
	AU 778294	B2	20041125	(200506)	EN	
	IN 2002CN00430	P4	20050304	(200547)	EN	
	US 20060100184	A9	20060511	(200633)	EN	
	EP 1224205	B1	20060510	(200634)	EN	
	DE 60027913	E	20060614	(200642)	DE	
	ES 2260055	T3	20061101	(200673)	ES	
	EP 1724279	A2	20061122	(200677)	EN	
	US 7138427	B2	20061121	(200677)	EN	
	US 20060276415	A1	20061207	(200681)	EN	
	DE 60027913	T2	20070111	(200707)	DE	

ADT WO 2001023406 A1 WO 2000-GB3737 20000929; US 20060100184 A9 CIP of WO 1999-GB951 19990326; US 7138427 B2 CIP of WO 1999-GB951 19990326; US 20060276415 A1 CIP of WO 1999-GB951 19990326; IN 2002CN00430 P4 WO 2000-GB3737; AU 2000075375 A AU 2000-75375 20000929; AU 778294 B2 AU 2000-75375 20000929; BR 2000014381 A BR 2000-14381 20000929; CN 1377368 A CN 2000-813606 20000929; DE 60027913 E DE 2000-627913 20000929; EP 1224205 A1 EP 2000-964439 20000929; EP 1224205 B1 EP 2000-964439 20000929; DE 60027913 E EP 2000-964439 20000929; ES 2260055 T3 EP 2000-964439 20000929; EP 1724279 A2 Div Ex EP 2000-964439 20000929; NZ 518596 A NZ 2000-518596 20000929; NO 2002001541 A WO 2000-GB3737 20000929; BR 2000014381 A WO 2000-GB3737 20000929; EP 1224205 A1 WO 2000-GB3737 20000929; US 20030004147 A1 CIP of WO 2000-GB3736 20000929; CZ 2002001114 A3 WO 2000-GB3737 20000929; JP 2003510332 W WO 2000-GB3737 20000929; MX 2002003305 A1 WO 2000-GB3737 20000929; NZ 518596 A WO 2000-GB3737 20000929; US 20060100184 A9 CIP of WO 2000-GB3737 20000929; EP 1224205 B1 WO 2000-GB3737 20000929; DE 60027913 E WO 2000-GB3737 20000929; US 7138427 B2 CIP of WO 2000-GB3737 20000929; US 20060276415 A1 CIP of WO 2000-GB3737 20000929; JP 2003510332 W JP 2001-526586 20000929; US 20060100184 A9 CIP of US 2001-647110 20010111; US 7138427 B2 CIP of US 2001-647110 20010111; CZ 2002001114 A3 CZ 2002-1114 20000929; IN

2002CN00430 P4 IN 2002-CN430 20020321; ZA 2002002382 A ZA 2002-2382 20020325; KR 2002092914 A KR 2002-703973 20020327 ; MX 2002003305 A1 MX 2002-3305 20020327; NO 2002001541 A NO 2002-1541 20020327; US 20030004147 A1 US 2002-109095 20020328; US 20060100184 A9 US 2002-109095 20020328; US 7138427 B2 US 2002-109095 20020328; US 20060276415 A1 Div Ex US 2002-109095 20020328; EP 1724279 A2 EP 2000-5867 20000929; US 20060276415 A1 US 2006-502784 20060811; DE 60027913 T2 DE 2000-627913 20000929; DE 60027913 T2 EP 2000-964439 20000929; DE 60027913 T2 WO 2000-GB3737 20000929

FDT AU 778294 B2 Previous Publ AU 2000075375 A; DE 60027913 E Based on EP 1224205 A; ES 2260055 T3 Based on EP 1224205 A; EP 1724279 A2 Div ex EP 1224205 A; NZ 518596 A Div in NZ 532211 A; AU 2000075375 A Based on WO 2001023406 A; BR 2000014381 A Based on WO 2001023406 A; EP 1224205 A1 Based on WO 2001023406 A; CZ 2002001114 A3 Based on WO 2001023406 A; JP 2003510332 W Based on WO 2001023406 A; MX 2002003305 A1 Based on WO 2001023406 A; NZ 518596 A Based on WO 2001023406 A; AU 778294 B2 Based on WO 2001023406 A; EP 1224205 B1 Based on WO 2001023406 A; DE 60027913 E Based on WO 2001023406 A; DE 60027913 T2 Based on EP 1224205 A; DE 60027913 T2 Based on WO 2001023406 A

PRAI GB 1999-23076 19990929
GB 1998-6513 19980326
GB 1999-5275 19990308

AB WO 2001023406 A1 UPAB: 20060117
NOVELTY - Sapogenin derivatives (I) and (II) and their stereoisomers and racemic mixtures, pro-drugs and salts are new.
DETAILED DESCRIPTION - Sapogenin derivatives of formula (I) and (II) and their stereoisomers and racemic mixtures, pro-drugs and salts are new.
R1 - R8, R10, = H, OH, =O, or OR; R = optionally substituted alkyl or acyl, carbamoyl or alkoxycarbonyl;
R9, R11 - R13 = H, OH, OR;
R14 = optionally substituted alkyl; R15, = H, optionally substituted alkyl, optionally substituted acyl or glucosyl;
dashed bond = optional double bond, but excluding in (I) where simultaneously R1 = R2 = R4 = R5 = R6 = R7 = R8 = R9 = R10 = R11 = R12 = R13 = H;
R3 = betaOH;
R14 = CH3;
the methyl group at C22 is alpha, the C20 is alpha, and there is a S configuration at C25.
INDEPENDENT CLAIMS are also included for: (1) use of (I) and (II) in the manufacture of a medicament for increasing the muscarinic receptor number or enhancing the function of muscarinic receptors;
(2) a pharmaceutical composition having cognitive function enhancing properties which comprises (I) or (II) in the form of an extract derived from a plant of the genus Smilax, Asparagus, Anemarrhena, Yucca or Agave;
(3) a non-therapeutic method of enhancing cognitive function; and (4) the use of (I) or (II) in a food product or beverage to enhance cognitive function.
ACTIVITY - Nootropic; Neuroprotective; Antiparkinsonian; Hypertensive.
MECHANISM OF ACTION - Increase muscarinic receptor number and function.
The effect of sapogenin derivatives on muscarinic receptor density in Chinese hamster ovary (CHO) cells expressing recombinant human muscarinic receptors was studied. CHO cells expressing high levels of receptor (approximately 2.2 moles receptor/mg protein) were cultured in flasks (150ml) for 24 hours before the start of the experiment. Vehicle (dimethylsulfoxide (DMSO)) and sapogenin derivative (at 1 and 10microM) were added to the medium for 48 hours. The culture medium was discarded, the cells scraped off and resuspended in Hanks solution, centrifuged and m-receptor levels determined by incubating with (3H)-QNB for 30 minutes followed by liquid scintillation counting. Protein levels were determined by a micro Lowry method. The results showed that over

the culturing period treatment with sapogenin derivatives prevents the decrease in muscarinic receptor number in a concentration-dependent manner. USE - The compounds can be used for increasing the muscarinic receptor number or enhancing the function of muscarinic receptors in a human or non-human animal (claimed). They can be used for treating cognitive dysfunction, Alzheimer's disease, senile dementia of the Alzheimer's type, Parkinson's disease, Lewi body dementia, postural hypotension, autism, chronic fatigue syndrome, myasthenia gravis, Lambert Eaton disease, diseases and problems associated with Gulf War syndrome, occupational exposure to organophosphorus compounds and problems associated with ageing (claimed). They can also be used to enhance cognitive function in a patient suffering from age-related cognitive dysfunction (claimed). They can be used to treat a condition characterized by the presence of neurofibrillary tangles and/or beta-amyloid plaques (claimed).

TECH ORGANIC CHEMISTRY - (I) and (II) can be prepared by synthetic methods from unsubstituted sapogenins. The reactions may involve the substitution of one OH-group by the functional radical desired, smilagenin and epismilagenin are preferred as starting products.

ABEX ADMINISTRATION - None given.
SPECIFIC COMPOUNDS - Two compounds are specifically claimed, i.e. 3-O-ethoxycarbonyl-5beta, 20alpha, 22alpha, 25R-spirostand-3beta-ol (3-beta-(ethoxycarbonyloxy)-5-alpha-androstano(16,17-b)-(4'-methyl-(5',2''-spiro)-(5''-methylpyrano)furan)) of formula (Ia) and epismilagenin succinate (3-alpha-(carboxyethylcarbonyloxy)-5-alpha-androstano(16,17-b)-(4'-methyl-(5',2''-spiro)-(5''-methylpyrano)furan)) of formula (Ib).
EXAMPLE - Ethyl chloroformate (1.40g) was added dropwise to a stirred solution of smilagenin (2.08g) in anhydrous dichloromethane (15ml) and anhydrous pyridine (1.02g). The mixture was stirred at room temperature for 18 hours and then partitioned between water (30ml) and dichloromethane. The aqueous layer was extracted twice with dichloromethane, the combined organic layers washed with water and then dried over MgSO4 (anhydrous). The solvent was evaporated in vacuo to give an oil (2.1g) that rapidly crystallized. This material was chromatographed on silica (ca. 70g). Elution with ethyl acetate-hexane (1:9) and recrystallization from methanol afforded white crystals of 3-O-ethoxycarbonyl-5beta, 20alpha, 22alpha, 25R-spirostand-3beta-ol (1.08g), m. pt. 154-156degreesC.

L55 ANSWER 9 OF 10 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
AN 2000-604069 [58] WPIX Full-text
CR 1999-496233; 2001-343159; 2001-541229; 2003-765551
DNC C2000-180835 [58]
DNN N2000-447105 [58]
TI Screening compound to assess effectiveness to treat receptor abnormalities in Alzheimer's disease by growing transfected cells beyond usual level to reach equilibrium, removing growth medium, adding test agent
DC B04; S03
IN HU Y; REES D; TOBIN A; XIA Z
PA (PHYT-N) PHYTOPHARM PLC
CYC 1
PIA GB 2347676 A 20000913 (200058)* EN 10[2] <--
ADT GB 2347676 A GB 1999-23075 19990929
PRAI US 1999-362328 19990728
GB 1999-5275 19990308
AB GB 2347676 A UPAB: 20050411
NOVELTY - Screening a compound (D) to determine its effectiveness to treat condition due to specific receptor (R) depletion, involves dividing cells transfected with (R) into control and test samples (CS; TS) which are grown in

nutrient medium (NM) to reach equilibrium state, removing (NM), adding test (D) dissolved in carrier to (TS) and carrier alone to CS, incubating (R) and determining number of (R).

DETAILED DESCRIPTION - Screening a compound (D) to determine its effectiveness to treat a condition due to specific receptor (R) depletion comprises: (a) preparing or retrieving suitable cells (C) (e.g. Chinese Hamster Ovary cells) transfected with DNA for the specific receptor or receptor type; (b) dividing the transfected (C) into two equal portions, one portion to serve as a control sample (CS) and the other to serve as a test sample (TS); (c) allowing the CS and the TS to grow in the presence of a nutrient medium (NM) until the (C) in the sample approach or reach a state of equilibrium; (d) removing the NM from both of the sample and then simultaneously adding to the TS the test (D) dissolved in a cytologically acceptable carrier and adding to the CS an equivalent concentration of the carrier; (e) incubating the (C) for a selected time and performing an assay to determine the numbers of (R) present in the (C) of the CS and the TS.

USE - (I) is useful for assessing the effectiveness of compounds for the treatment of conditions caused by deficiency in number or function of membrane bound receptors and also for assessing compounds for treatment of cognitive dysfunction conditions, including Alzheimer's disease and senile dementia.

TECH BIOTECHNOLOGY - Preferred Method: In (I) the transfected (C) are allowed to reach at least 80% confluence in the step of growing the sample in NM. The incubation period is at least 72 hours.

ABEX EXAMPLE - Chinese Hamster Ovary (CHO) cells transfected with DNA for the human m2 muscarinic receptor expressed high levels of m2 receptors. Frozen cells were removed and plated out onto dishes or flasks and a conventional growth medium containing cell nutrients including fetal calf serum and/or other appropriate nutrient factors) was added. To the test samples a medium containing the test compound dissolved in a cytologically acceptable carrier medium was added and for the control samples, an identical medium except that it contained none of the test compound was added and the medium was removed. Cells were plated on well plates 24 hours before the experiment and were allowed to grow till they reached at least 80% confluence. The medium was then removed and replaced with medium containing vehicle only Dimethyl sulfoxide (DMSO) or medium containing the same vehicle carrying a test compound e.g. sarsasapogenin (10mM). The cells were then incubated. It was found that the number of m2 receptor increased when compared to the control on prolong incubation with sarsasapogenin.

L55 ANSWER 10 OF 10 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
AN 1999-496233 [42] WPIX Full-text
CR 2000-604069; 2001-343159; 2001-541229; 2003-765551
DNC C1999-145657 [42]
TI Composition having cognitive function enhancing properties used to treat e.g. Alzheimer's disease
DC B04
IN BROSTOFF J; GUNNING P; HU Y; MAXTED S K; RUBIN I; RUBIN L; WANG W; WHITTLE B; WHITTLE B A; WNAG W; XIA Z; YAER H; ZONGQIN X; BROSTOFFJONATHAN; GUNNINGPHIL; HUYAER; RUBINIAN; WANGWEIJUN; WHITTLEBRIAN; XIAZONGQIN
PA (BROS-I) BROSTOFF J; (GUNN-I) GUNNING P; (HUYY-I) HU Y; (PHYT-N) PHYTOPHARM P/C; (PHYT-N) PHYTOPHARM PLC; (RUBI-I) RUBIN I; (WANG-I) WANG W; (WHIT-I) WHITTLE B; (XIAZ-I) XIA Z; (NATU-N) NATURAL INPUT SOLUTIONS INC
CYC 85
PIA GB 2335599 A 19990929 (199942)* EN 35[0] <--
WO 9948482 A2 19990930 (199948) EN <--
WO 9948507 A2 19990930 (199948) EN <--

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JP 2004224797	A	20040812	(200453)	JA	17	
US 6812213	B2	20041102	(200472)	EN		
RU 2242978	C2	20041227	(200510)	RU		
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ES 2272060	T3	20070416	(200728)	ES		
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KR 2007007214	A	20070112	(200755)	KO		
US 20070191290	A1	20070816	(200755)	EN		
KR 632052	B1	20061004	(200759)	KO		

MX 243092 B 20070108 (200760) ES
ADT GB 2335599 A GB 1999-7100 19990326; AU 9931574 A AU 1999-31574 19990326; AU 748138 B AU 1999-31574 19990326; AU 2002027740 A Div Ex AU 1999-31574 19990326; AU 781810 B2 Div Ex AU 1999-31574 19990326; AU 9931581 A AU 1999-31581 19990326; BR 9909109 A BR 1999-9109 19990326; BR 9909110 A BR 1999-9110 19990326; CN 1302208 A CN 1999-806042 19990326; CN 1209112 C CN 1999-806042 19990326; CN 1301166 A CN 1999-806158 19990326; CN 1679591 A Div Ex CN 1999-806158 19990326; CN 1198622 C CN 1999-806158 19990326; DE 69929177 E DE 1999-629177 19990326; DE 69929177 T2 DE 1999-629177 19990326; DE 69933016 E DE 1999-633016 19990326 ; DE 69933016 T2 DE 1999-633016 19990326; EP 1066042 A2 EP 1999-913453 19990326; EP 1066042 B1 EP 1999-913453 19990326 ; DE 69933016 E EP 1999-913453 19990326; EP 1719512 A2 Div Ex EP 1999-913453 19990326; DE 69933016 T2 EP 1999-913453 19990326; ES 2272060 T3 EP 1999-913453 19990326; EP 1066033 A1 EP 1999-913462 19990326; EP 1066033 B1 EP 1999-913462 19990326; DE 69929177 E EP 1999-913462 19990326; ES 2257042 T3 EP 1999-913462 19990326; DE 69929177 T2 EP 1999-913462 19990326; GB 2335599 B GB 1999-7100 19990326; IL 138663 A IL 1999-138663 19990326; NZ 507355 A NZ 1999-507355 19990326; WO 9948482 A2 WO 1999-GB960 19990326; WO 9948507 A2 WO 1999-GB951 19990326; NO 2000004804 A WO 1999-GB951 19990326; BR 9909109 A WO 1999-GB951 19990326; BR 9909110 A WO 1999-GB960 19990326; NO 2000004803 A WO 1999-GB960 19990326; EP 1066033 A1 WO 1999-GB960 19990326; EP 1066042 A2 WO 1999-GB951 19990326; CZ 2000003538 A3 WO 1999-GB960 19990326; CZ 2000003541 A3 WO 1999-GB951 19990326; HU 2001001693 A2 WO 1999-GB951 19990326; JP 2002507572 W WO 1999-GB951 19990326; HU 2001003654 A2 WO 1999-GB960 19990326 ; US 20030118673 A1 Cont of WO 1999-GB960 19990326; JP 2003524581 W WO 1999-GB960 19990326; MX 2000009437 A1 WO 1999-GB960 19990326; NZ 507355 A WO 1999-GB951 19990326; RU 2242978 C2 WO 1999-GB951 19990326; IN 2000CN00543 P4 WO 1999-GB951 19990326; IN 2000CN00533 P4 WO 1999-GB960 19990326 ; EP 1066033 B1 WO 1999-GB960 19990326; DE 69929177 E WO 1999-GB960 19990326; JP 3768100 B2 WO 1999-GB951 19990326; DE 69929177 T2 WO 1999-GB960 19990326; EP 1066042 B1 WO 1999-GB951 19990326; DE 69933016 E WO 1999-GB951 19990326; DE 69933016 T2 WO 1999-GB951 19990326; KR 2007007214 A WO 1999-GB960 19990326; KR 632052 B1 WO 1999-GB951 19990326; IN 2000MN00533 P3 WO 1999-GA325 19990423; US 6258386 B1 US 1999-362328 19990728; US 20010043955 A1 Div Ex US 1999-362328 19990728; US 20030032604 A1 Div Ex US 1999-362328 19990728; US 20040081709 A1 Div Ex US 1999-362328 19990728; US 7166308 B2 Div Ex US 1999-362328 19990728; US 20070191290 A1 Cont of US 1999-362328 19990728; CZ 2000003538 A3 CZ 2000-3538 19990326; CZ 2000003541 A3 CZ 2000-3541 19990326; JP 2003524581 W JP 2000-537532 19990326; JP 2002507572 W JP 2000-537555 19990326; JP 2004217666 A Div Ex JP 2000-537555 19990326; JP 2004224797 A Div Ex JP 2000-537555 19990326; JP 3768100 B2 JP 2000-537555 19990326; RU 2242978 C2 RU 2000-126789 19990326; RU 2297228 C2 Div Ex RU 2000-126789 19990326; KR 2001042190 A KR 2000-710677 20000926; KR 632052 B1 KR 2000-710677 20000926; KR 2001042205 A KR 2000-710698 20000926; MX 2000009437 A1 MX 2000-9437 20000926 ; MX 2000009441 A1 MX 2000-9441 20000926; NO 2000004803 A NO 2000-4803 20000926; NO 2000004804 A NO 2000-4804 20000926; IN 2000CN00533 P4 IN 2000-CN533 20001017; IN

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FDT AU 781810 B2 Previous Publ AU 2002027740 A; AU 748138 B Previous Publ AU 9931574 A; AU 2002027740 A Div ex AU 748138 B; DE 69929177 E Based on EP 1066033 A; ES 2257042 T3 Based on EP 1066033 A; DE 69929177 T2 Based on EP 1066033 A; DE 69933016 E Based on EP 1066042 A; EP 1719512 A2 Div ex EP 1066042 A; DE 69933016 T2 Based on EP 1066042 A; ES 2272060 T3 Based on EP 1066042 A; JP 3768100 B2 Previous Publ JP 2002507572 W; KR 632052 B1 Previous Publ KR 2001042190 A; US 20010043955 A1 Div ex US 6258386 A; US 20030032604 A1 Div ex US 6258386 B; US 20040081709 A1 Div ex US 6258386 B; US 7166308 B2 Div ex US 6258386 B; US 20070191290 A1 Cont of US 6258386 B; US 20060182817 A1 Cont of US 6812213 B; US 20070191290 A1 Cont of US 7166308 B; AU 9931581 A Based on WO 9948482 A; BR 9909110 A Based on WO 9948482 A; EP 1066033 A1 Based on WO 9948482 A; CZ 2000003538 A3 Based on WO 9948482 A; HU 2001003654 A2 Based on WO 9948482 A; JP 2003524581 W Based on WO 9948482 A; MX 2000009437 A1 Based on WO 9948482 A; EP 1066033 B1 Based on WO 9948482 A; DE 69929177 E Based on WO 9948482 A; DE 69929177 T2 Based on WO 9948482 A; KR 2007007214 A Based on WO 9948482 A; AU 9931574 A Based on WO 9948507 A; BR 9909109 A Based on WO 9948507 A; EP 1066042 A2 Based on WO 9948507 A; CZ 2000003541 A3 Based on WO 9948507 A; HU 2001001693 A2 Based on WO 9948507 A; JP 2002507572 W Based on WO 9948507 A; AU 748138 B Based on WO 9948507 A; NZ 507355 A Based on WO 9948507 A; RU 2242978 C2 Based on WO 9948507 A; JP 3768100 B2 Based on WO 9948507 A; EP 1066042 B1 Based on WO 9948507 A; DE 69933016 E Based on WO 9948507 A; IL 138663 A Based on WO 9948507 A; DE 69933016 T2 Based on WO 9948507 A; KR 632052 B1 Based on WO 9948507 A; MX 243092 B Based on WO 9948482 A

PRAI GB 1998-5275 19980308
GB 1998-6513 19980326
AU 2002-27740 20020327
US 1998-82946P 19980424

US 1998-113352P 19981221

AB GB 2335599 A UPAB: 20060115

NOVELTY - Composition having cognitive function enhancing properties comprises a saponin or sapogenin.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (A) the use of an extract of a plant of the genus Smilax, Asparagus, Anemarrhena, Yucca, or Agave in a medicament having cognitive function enhancing properties; and (B) treatment of a condition characterized by a deficiency in membrane-bound receptor number or function in a tissue, organ, cell type or organelle, comprising, modulating the action of a cytostolic, nuclear or membrane-bound protein or receptor which, when activited by an agonist binding to it, or when its activity is promoted by deactivation of an antagonist, upregulates and/or normalizes the number and/or turnover of membrane-bound receprots in that tissue, organ, cell type or organelle. ACTIVITY - Nootropic; neuroleptic; antiparkinsonian.

MECHANISM OF ACTION - The compositions give increased levels of membrane-bound receptor mRNA, specifically m1 receptor mRNA. 20 Month old pure-line male SD rats were divided randomly into 2 groups. One group received 3 mg of sarsasapogenin per rat per day mixed into the daily feed. The control group received normal food and water. 4 Months later, their brains were used in hybridization technique experiments with 4-6 months old rats used as a young control group. Other feeding arrangements for each group were completely identical. The rats were decapitated and their brains removed intact. Coronal slices (15 micro m thick) were prepared. Studies showed that there was a significant reduction on mRNA expression for m1 receptors in the striatum of aged rats compared to young controls. Administration of sarsasapogenin resulted in a significant increase in m1 receptor mRNA in the same brain area when treated animals were compared to aged, untreated controls.

USE - The composition is used to enhance cognitive function, preferably for the treatment of conditions characterized by a deficiency in postsynaptic membrane-bound receptor number or function, especially Alzheimer's disease or senile dementia of the Alzheimer's type (all claimed).

Other conditions which can be treated include Parkinson's disease, Lewi body dementia, postural hypotension, autism, chronic fatigue syndrome, Myasthenia Gravis, Lambert Eaton disease, diseases and problems associated with Gulf War Syndrome, occupation exposure to organophosphorus, and problems associated with ageing.

ADVANTAGE - The substances used do not have high overt estrogenic, androgenic and/or anabolic activity in patients.

TECH

PHARMACEUTICALS - Preferred Composition: The saponin or sapogenin is a steroinal saponin or sapogenin, preferably non-estrogenic.

The saponin or sapogenin is derived from a plant of the genus Smilax, Asparagus, Anemarrhena, Yucca, or Agave. The composition contains: at least two of sarsasapogenin, smilagenin, prazerigen, an astragaloside, tigogenin, hecogenin, and diosgenin ; one or more of smilagenin, prazerigen, an astragaloside, tigogenin, hecogenin, and diosgenin; or smilagenin, anzurogenin D or an astragaloside.

BIOTECHNOLOGY - Preferred Treatment: In (B) the protein or receptor, when activated, increases the amount of mRNA molecules in the tissue, organ, cell type, or organelle which code for membrane bound receptors. This works by increasing the production, transcription or expression, or decreasing the breakdown of the mRNA molecules.

The protein or receptor, when activated modulates the expression of the DNA in the tissue, organ, cell type, or organelle which code for membrane bound receptors.

The protein or receptor, when activated upregulates and/or normalizes the number and/or turnover of muscarinic and/or adrenergic receptors in that tissue, organ, cell type, or organelle.

The action of the receptor is modulated by administration of a substance which is at least a partial agonist of nicotinic receptors. The agonist is preferably saponin or sapogenin, especially sarsasapogenin, smilagenin, prazerigen, an astragaloside, tigogenin, hecogenin, or diosgenin.
The receptor is located in the cytosol of the cells of the tissue, organ, cell type, or organelle. The receptor is a steroid receptor, preferably an estrogen receptor.

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               E TIFFIN/AU
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               E GUNNING/PA
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L5            21 S E3-E7
               E PHYTOTECH/PA
L6            19 S E3-E5
               E PHYT/PACO
               E E7+ALL
L7            50 S L1-L6
L8            16 S L7 AND C07J/IPC,IC,ICM,ICS
L9           267 S ?SAPOGENIN?
L10         1971 S C07J071/IPC,IC,ICM,ICS
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L12           30 S (RA936W OR RA0MNJ OR RA936V OR RA0MNI)/DCN
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               E DIOSGENON/CN
               E DIOSGENIN/CN
L15            1 S E3
L16            1 S E4
L17          197 S R01308/DCN OR 1308/DRN OR DIOSGENIN?
L18           92 S RA1A08/DCN OR DIOSGENIN? GLUCOSIDE OR DISOGLUSIDE OR ALLIUMOS
L19         2372 S L14,L17,L18
               E DIOSGENONE/BI,ABEX
L20            7 S E1-E3,E5,E6
               E BACK E1
L21          187 S E3-E5
L22            2 S E8,E9
L23         2373 S L19-L22
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L36           1 S L32 AND (A313(S)Q509)/M0,M1,M2,M3,M4,M5,M6
L37           1 S L32 AND Q509/M0,M1,M2,M3,M4,M5,M6
L38           1 S L32 AND (RA34QM OR RA0O9I OR RA7BP2 OR RA34QR OR RAE8H6 OR RA
L39           4 S L32 AND (ORGANOBORAN? OR ORGANOALUMIN? OR ORGANO () (BORAN? O
L40           3 S L39 NOT L34-L38
L41           1 S L34-L39 NOT L40
L42          31 S L32 AND N412/M0,M1,M2,M3,M4,M5,M6
L43          16 S L42 AND (N243(S)N412)/M0,M1,M2,M3,M4,M5,M6
L44          13 S L42 AND (N243(S)N412(S)N362)/M0,M1,M2,M3,M4,M5,M6
L45           7 S L44 NOT VITAMIN D#
L46           6 S L45 NOT L41
L47           9 S L43 NOT L45
L48           2 S L47 NOT VITAMIN D#
L49          15 S L42 NOT L43-L48
L50          11 S L49 NOT VITAMIN D#
L51          12 S L7 AND L23
L52          17 S L8,L51
L53          10 S L52 AND L32,L33
L54          10 S L41,L53
L55          10 S L54 AND L1-L54
L56           7 S L52 NOT L55

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